

### **REMARKS**

Claims 178-183 are pending in this application. Claim 179 is amended herein. Support for these amendments can be found throughout the specification. No new matter has been introduced.

In view of these amendments and the remarks that follow, Applicant submits that the application is now in condition for allowance and an early action to that effect is respectfully requested.

### **Priority**

In the Final Office Action dated October 28, 2010 (hereinafter, "Office Action"), Applicant notes the Examiner's assertion that the pending claims are not supported by the disclosure of priority application no. 60/037921, filed February 12, 1997, and will be afforded the filing date of the priority application no. 60/064,687, filed November 5, 1997. Without acquiescing with the Examiner's statements, Applicant notes that the prior art rejections are based on art published in 1995, more than a year before either priority date, and thus the determination of priority for these claims has no bearing on the current prior art rejections.

### **Information Disclosure Statement**

Filed herewith is an Information Disclosure Statement to update the information of record in this application. The Examiner is respectfully requested to consider the information cited therein and initial the Form SB08 to confirm her consideration of this information.

### **Claim Rejections under 35 U.S.C. § 103(a)**

#### **(a) Rejection of Claims 178-182 over Yin in view of Nie**

Claims 178-182 stand rejected under 35 U.S.C. § 103(a) as being allegedly obvious over Yin et al., Science (1995) 270:1653-1657 ("Yin"), in view of Nie et al., Anal. Chem. (1995) 76(17): 2849-2857 ("Nie"). *See* Office Action at pages 3-5. According to the Examiner, Yin teaches all of the elements of claims 178-182 except for labeling with a unit specific marker. *See, e.g.*, Office Action at page 4 (acknowledging that Yin "does not teach labeling with a unit

specific marker”). However, the Examiner contends that this missing element is supplied by Nie, which allegedly discloses use of a unit specific marker. *See* Office Action at page 4.

Applicant respectfully traverses and submits that the proposed combination of Yin and Nie, even if proper, does not render claims 178-182 obvious because this combination does not yield at least one element of the rejected claims, *i.e.*, use of a unit specific marker, and the Examiner has failed to establish a *prima facie* case of obviousness for this missing element. The specification explains that a unit specific marker is “a compound which specifically interacts with one or more units of the polymer and is capable of identifying those units.” *See* Specification as filed, page 73, lines 8-10. The Examiner characterizes Nie as disclosing a unit specific marker at page 2561, col. 1 and Figure 8. *See, e.g.*, Office Action at page 4. Applicant respectfully disagrees and submits that Nie nowhere discloses the use of a unit specific marker. For example, Figure 8 of Nie discloses, *inter alia*, the observation of “fluorescence signals from a  $\lambda$ -DNA molecule labeled with the bis-intercalating fluorescent dye YOYO”; similarly, page 2581 describes “[f]luorescent labeling of DNA...by adding a small volume of nucleic acid sample to an oxazole yellow homodimer (YOYO) solution”. (Although the Examiner cited page 2651 of Nie, Nie does not include any such page; Applicant assumes for purpose of this response that the Examiner instead meant to cite to page 2851 of Nie). Review of these cited portions confirms that Nie only disclose the use of YOYO, an intercalating dye that *non-specifically* interacts with the nucleic acid molecule and that is *not* capable of identifying the unit to which it binds. Applicant respectfully submits that the Examiner has failed to establish a *prima facie* case of obviousness because the Examiner has not articulated any reasoning whatsoever to support a finding that inclusion of the missing element would have been obvious to the skilled artisan at the time of filing. *See, e.g.*, MPEP § 2142 (“The key to supporting any rejection under 35 U.S.C. § 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious.”)

Furthermore, even assuming *arguendo* that the YOYO dye could be somehow construed to be a unit-specific marker (which it is clearly not), the Examiner’s rejection is still misplaced for the additional and separate reason that the teachings of Yin and Nie are incompatible and cannot be combined in the manner suggested by the Examiner, otherwise Yin would be rendered unsatisfactory for its intended purpose. Yin discloses the use of “a microscope based optical trapping interferometer” to measure the mechanical force, termed  $F_{tc}$ , exerted by a stationary

polymerase on a bead linked to the polymerase through a nucleic acid template, where the bead is held within an optical trap exerting an opposing force  $F_{\text{trap}}$  on the bead. *See* Yin at page 1654. The purpose to be achieved in Yin, *i.e.*, measuring the force  $F_{\text{tc}}$  exerted by the polymerase on the bead, cannot be accomplished by using a unit specific marker to label the nucleic acid template, since it is the relative displacement of the *bead* (not of the template) that is observed and assessed in the method of Yin. Accordingly, there would be no motivation to include a unit specific marker in the system of Yin, since no useful result could be accomplished thereby. Because the proposed modification would render Yin unsatisfactory for its intended purpose, Applicant respectfully submits that the Examiner has failed to establish a *prima facie* case of obviousness. *See, e.g.*, MPEP § 2143.01, section V (citing *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984)) (“If [the] proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification.”).

Finally, the Examiner’s rejection is also misplaced for the separate and independent reason that inclusion of a unit specific marker within the system of Yin would defect the principle of operation of Yin, which is to measure the mechanical force  $F_{\text{tc}}$  exerted by the polymerase by observing the resulting displacement of a bead linked to the polymerase. Because the proposed combination would change the principle of operation of Yin, Applicant respectfully submits that the Examiner has failed to establish a *prima facie* case of obviousness. *See, e.g.*, MPEP § 2143.01, section VI (citing *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959)) (“If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious.”)

For at least these reasons, Applicant respectfully requests reconsideration and withdrawal of the rejection of claims 178-182 under 35 U.S.C. § 103 as obvious over Yin in view of Nie.

(b) Rejection of Claims 180-181 and 183 over Yin in view of Nie and Vurek

Claims 180-181 and 183 stand rejected under 35 U.S.C. § 103(a) as being allegedly obvious over Yin in view of Nie as applied to claims 178-179 and 182, and further in view of Vurek. *See* Office Action at pages 5-6. According to the Examiner, Yin teaches all of the elements of claims 180-181 and 183 except for labeling with a unit specific marker or the use of

a waveguide, whereas Nie allegedly discloses the use of a unit specific marker and Vurek allegedly discloses the use of a waveguide. *See* Office Action at pages 5-6.

Applicant respectfully traverses and submits that the proposed combination of Yin, Nie and Vurek, even if proper, does not render claims 180-181 or 183 obvious because this combination does not yield at least one element of the rejected claims, *i.e.*, the use of a unit specific marker, and the Examiner has failed to establish a *prima facie* case of obviousness for this missing element. The teachings of Yin and Nie are discussed above; at a minimum, neither Yin nor Nie teaches or suggests the use of a unit specific marker. Vurek cannot remedy this deficiency because Vurek nowhere teaches or suggests the use of a unit specific marker. Applicant respectfully submits that the Examiner has failed to establish a *prima facie* case of obviousness because the Examiner has not articulated any reasoning whatsoever to support a finding that inclusion of the missing element would have been obvious to the skilled artisan at the time of filing. *See, e.g.*, MPEP § 2142 (“The key to supporting any rejection under 35 U.S.C. § 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious.”)

Furthermore, even assuming *arguendo* that Nie or Vurek could somehow be construed to disclose a unit-specific marker (which they clearly do not), the Examiner’s rejection is misplaced for the additional and separate reason that the teachings of Yin are incompatible with the teachings of Nie and/or Vurek and cannot be combined in the manner suggested by the Examiner, otherwise Yin would be rendered unsatisfactory for its intended purpose. As discussed above, no useful result could be accomplished by including a unit specific marker in the system of Yin. Furthermore, no useful result could be accomplished by positioning the system of Yin within a waveguide as disclosed by Vurek, since Yin requires the use of an optical trap, not a waveguide. Because the proposed modifications would render Yin unsatisfactory for its intended purpose, Applicant respectfully submits that the Examiner has failed to establish a *prima facie* case of obviousness. *See, e.g.*, MPEP § 2143.01, section V (citing *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984)) (“If [the] proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification.”).

Finally, the Examiner’s rejection is misplaced for the separate and independent reason that inclusion of a unit specific marker and/or a waveguide within the system of Yin would

defect the principle of operation of Yin, which is to measure the mechanical force  $F_{tc}$  exerted by the polymerase by observing the resulting displacement of a bead linked to the polymerase. Because the proposed combination would change the principle of operation of Yin, Applicant respectfully submits that the Examiner has failed to establish a *prima facie* case of obviousness. See, e.g., MPEP § 2143.01, section VI (citing *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959)) (“If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious.”)

For at least these reasons, Applicant respectfully requests reconsideration and withdrawal of the rejection of claims 180-181 and 183 under 35 U.S.C. § 103 as obvious over Yin in view of Nie and/or Vurek.

### CONCLUSION

In view of the amendments and remarks made herein, Applicant respectfully submits that the application is now in condition for allowance, and an early action to that effect is respectfully solicited. An interview with the Examiner to discuss the outstanding rejections is respectfully requested, and the Examiner is invited to contact the undersigned agent at the telephone number provided below.

Applicant hereby authorizes the Commissioner to charge any additional fees that may be required in connection with this application and/or to credit overpayment to **Deposit Account No. 50-3994**. In the event that additional fees or extensions of time are required, Applicant herein petitions for the necessary extension of time under 37 C.F.R. § 1.136(a) and authorizes the Commissioner to charge these fees or credit any overpayment associated with this or any other filing to this deposit account. This is not an authorization to pay the issue fee.

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Respectfully submitted,

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